A DISSERTATION ON COMPARISON OF FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGY IN THYROID DISEASE

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CERTIFICATE

This is to certify that the dissertation entitled "**COMPARISON OF FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGY IN THYROID DISEASE"** is the bonafide original work of Dr**. S. Nirmala Devi** under the guidance of **Dr. Bhavani Shankar MS.,** Prof. General Surgery SIII unit KMCH, Chennai in partial fulfillment of the requirements for MS (General Surgery) branch II examination of the Tamil Nadu Dr. M.G.R Medical university to be held in March 2010. The period of postgraduate study and training was from May 2007 to March 2010.

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LIST OF ABBREVIATIONS

1. FNAC	-	FINE NEEDLE ASPIRATION CYTOLOGY
2. HPE	-	HISTOPATHOLOGY
3. RLN	-	RECURRENT LARYNGEAL NERVE
4. TSH	-	THYROID STIMULATING HORMONE
5. ATP	-	ADENOSINE TRIPHOSPHATE
6. CEA	-	CARCINO EMBRYONICANTIGEN
7. USG	-	ULTRASONOGRAM
8. PTC	-	PAPILLARY THYROID CARCINOMA
9. MTC	-	MEDULLARY THYROID CARCINOMA
10.MEN	-	MULTIPLE ENDOCRINE NEOPLASIA
11.CT	-	COMPUTED TOMOGRAM
12.RHT	-	RIGHT HEMI THYROIDECTOMY
13.LHT	-	LEFT HEMI THYROIDECTOMY
14.STT	-	SUBTOTAL THYROIDECTOMY
15.D.O.S	-	DATE OF SURGERY
16.CA	-	CARCINOMA
17.MNG	-	MULTINODULAR GOITER.
18.RT SNG	-	RIGHT SOLITARY NODULAR GOITER
19.LT SNG	-	LEFT SOLITARY NODULAR GOITER
20.NCG	-	NODULAR COLLOID GOITER

CONTENTS

INTRODUCTION

INTRODUCTION

A thyroid nodule is a palpable swelling in a thyroid gland with an otherwise normal appearance. Prevalence ranges from 4% to 10% in general adult and 0.2 to 1.5% in children. Nodular, goiters are more common in women because of the presence of oestrogen receptors in thyroid issue.

Most of the nodules are benign and only 5 to 10% of these nodules are malignant.

Many tests and procedures are available for evaluation of thyroid nodules. Among them FNAC is the initial investigation in euthyroid nodules. The incidence of malignant disease in cold nodule varies form 9% to 35% and the incidence of carcinoma in cystic lesion <4cm in size is less than 2%

AIM OF THE STUDY

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The purpose of this study was

1. To observe the correlation of FNAC and histopathology in various thyroid disorders.

    Solitary nodular goiter

    Multi nodular goiter

    Suspected malignancy of thyroid

    malignancy of thyroid

2. To stress the importance of HPE as final diagnostic tool.

3. The role of surgery as diagnostic as well as therapeutic.

REVIEW OF LITERATURE

DEVELOPMENT

Thyroid develops from median endodermal diverticulum during 4th week of embryologic development. It descends from foramen ceacum in front of pharynx as a bilobed diverticulum. By the end of 2nd month thyroid reaches its final position in front of trachea. The lower end of the diverticulum enlarges to form gland and the rest ie thyroglossal duct disappears. The lower end persists as pyramidal lobe.

ANATOMY

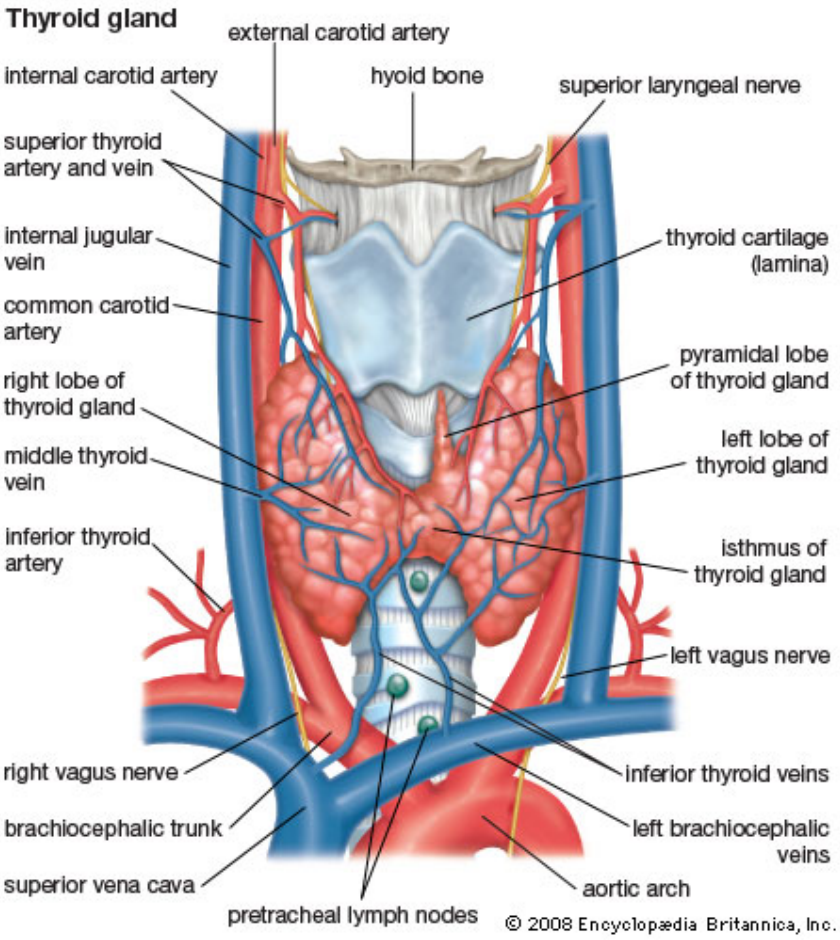
The normal thyroid gland is light brown in colour and weighs approximately 20gm. Thyroid gland consists of right and left lobes that are joined to each other by the isthumus . A pyramidal lobe which represents the most caudal end of thyroglossal duct is found in approximate by 50% of individuals

Each lobe measures about 5x2.5cmx2.5cm and isthmus 1.2x1.2cm There are two capsules for thyroid gland. True capsule is the peripheral condensation of the connective tissue of the gland.

The false capsule is derived from the pretracheal layer of deep cervical fascia. It is thin along the posterior border of the lobes. It is thick on the inner surface of the gland where it forms a suspensory ligament (of Berry) which connects the lobe to cricoid cartilage

The lobes are conical in shape. Each lobe has medial surface, lateral or superficial surface and posterolateral or posterior surface and two borders anterior and posterior.

ANATOMY OF THYROID GLAND



ARTERIAL SUPPLY:-

- Paired superior thyroid arteries
- Paired inferior thyroid arteries
- Thyroidea ima artery
- Small branches from Laryngeal and tracheoesophageal arteries

The superior thyroid artery is the first anterior branch of the external carotid artery. It runs inferiorly to reach the superior pole of the gland. It runs close to external laryngeal nerve. It divides into anterior and posterior Branch.

Inferior thyroid artery is a branch of the thyrocervical trunk (which arises form the subclavian artery) It runs superiorly behind the carotid artery arches medially to reach lower pole of gland. Its terminal part is intimately related to recurrent laryngeal nerve. The artery divides into 4 or 5 glandular branches which pierces fascia and supply lower part of gland.

Superior thyroid artery supplies upper 1/3 of lobe and upper ½ of isthmus and inferior thyroid artery supplies lower 2/3 of lobe and lower half of the isthmus.

Thyroidea ima artery other name lowest thyroid artery arises from arch of aorta or from brachio cephalic trunk.

VENOUS DRAINAGE:-

Superior thyroid vein emerges at the upper pole and drains into internal jugular vein. Middle thyroid vein drains into internal jugular vein. Inferior thyroid vein drains into brachio cephalic vein.

LYMPHATIC DRAINAGE:-

Upper part of the gland drains into upper deep cervical (directly (or) via prelaryngeal nodes)

Lower part of the gland - Pre Tracheal nodes

Para tracheal nodes

Lower deep cervical nodes

But within the gland lymphatics form a plexus through which lymph may pass in any direction

NERVE SUPPLY

Sympathetic: - superior and middle cervical sympathetic ganglia fibres enter with blood vessels and are vasomotor.

PARASYMPATHETIC:-

From vagus nerve, fibres reach gland thro laryngeal nerve.

LARYNGEAL NERVES:-

The left RLN arises from the vagus nerve where it crosses aortic arch loops around ligamentum arteriosum and runs towards tracheoesophageal groove.

Right RLN arises from vagus at its crossing with right subclavian artery. The Right RLN may be non recurrent in 0.5 to 1 % of people and associated with vascular anomaly. The Left RLN rarely non recurrent in cases with situs inversus and right sided aortic arch.

Superior laryngeal nerves arise from vagus nerve. Arises at the level of base of skull and travels along internal carotid artery and divides into two braches internal and external at the level of hyoid bone.

Internal branch is sensory to supraglottic larynx and injury results in aspiration. External branch runs alongside the superior thyroid vessels before innervation of cricothyroid muscle. In 20% of people this nerve crosses below the tip of superior pole and increased liability for injury. This nerve is also called as Amelita Galla curci or “high note” nerve after the opera singer. Injury results in difficulty in hitting high notes projecting the voice and voice fatigue during prolonged speech.

PHYSIOLOGY

The average daily requirement of Iodine is 100 μmg/day. Fish, milk, egg, as additives in salt/ bread are the sources of iodine. Iodine is converted to iodide and rapidly absorbed from stomach and jejunum and distributed throughout the extra cellular space but mostly concentrated in thyroid gland by an active process.

SYNTHESIS OF THYROID HORMONE

I) Iodide trapping:-

- Active ATP dependant process across basement membrane of thyrocyte
- Enzyme dehalogenase
- Concentrated in thyroid follicular cells

II) Oxidation of iodide to iodine and iodination of tyrosine residues on Thyroglobulin to form monoiodo tyrosine (MITs) and diiodo tyrosine (DITS)

- The enzyme involved in this step is peroxidase at apical membrane

III Coupling

Formation of tetraiodo thyronine or thyroxine (T4) from two DITS

Formation of triodothyronine from one MIT& one DIT

Thyroglobulin carrying T4 and T3 is then internalized by pinocytosis is digested in lysosomes.

IV) Thyroglobulin hydrolyses to release free T3 and T4 and MITS and DITS. The latter are deiodinated and recycled.

Thyroid hormones are transported in serum bound to carrier proteins like thyroxin binding globulin (TIBG) thyroxinebinding prealbumin (TBPA) and albumin

T3 is more active than T4. T3 is less tightly bound to proteins. Half life of T3 is 1 day whereas of Half life T4 is 7 days

About 75% of total T3 is derived from peripheral conversion from T4 is liver, muscles, kidney, anterior pituitary and catalyses by 5' mono deiodinase.

After tissue utilization, the hormones are deiodinated and the released iodine enters the metabolic pool. Residual hormones are conjugated with glucuronic acid and excreted in urine and bile

TSH is secreted by the anterior pituitary under the influence of TRH secreted by hypothalamus.

INVESTIGATION

THYROID FUNCTION TESTS :-

Serum T3, T4, TSH serum TSH –most sensitive and specific to find hypo or hyper function normal value 0.5 to 5.5 munits /m/ L

Free T3 - 3 to 9 pmol/l

Free T4 - 12 to 28 pmol/lt

Total T3 - 1.5 to 3.5 nmol/L

Total T4 - 55 to 150 nmol/l

THYROID AUTO ANTIBODIES:-

In graves disease-TSH receptor antibodies are elevated

In Hashimoto's – Thyroglobulin antibodies

Thyroid peroxidase antibodies

Both are elevated

TUMOR MARKERS:-

Serum calcitonin – medullary carcinoma

Serum thyroglobulin – residual or recurrent disease after surgery for differentiated cancers.

RADIOLOGY (XRAY):-

Calcification is typical of psammoma bodies of papillary carcinoma maybe visible in plain xray. But calcification in xray neck is not diagnostic of malignancy.

Others like tracheal shift, scabbard trachea, calcified lesion of tuberculous adenitis can also be seen.

ULTRASOUND NECK :-

Brightness – mode ultrasound is the most sensitive test to detect lesions in the thyroid. It accurately measures the dimensions, identifies structures and evaluates diffuse changes in the thyroid parenchyma. It is non invasive and relatively inexpensive and can identify nodules not apparent on physical examination, isotope scanning or other imaging techniques.

It should not be used as a substitute for physical examination. It is not indicated as screening test in general population. Because of high prevalence of small, clinically inapparent thyroid nodules and the minimal aggressiveness of most thyroid cancers, ultrasound should be used as a screening test only if well known risk factors are present

INDICATIONS :- (8)

- In a patient who has a palpable nodule
- In a patient who has history of radiation
- In a patient who has family history of medullary carcinoma thyroid.
- If unexplained cervical adenopathy is present.

OTHER IMAGING TECHNIQUES

MRI and CT are not recommended for routine use because they are rarely diagnostic for malignancy in nodular thyroid disease and costly.

They are useful to assess size , substernal extension and positional relationship of goiter to surrounding structures

We should be cautious while using CT contrast medium that contains iodine because it decreases subsequent iodine 131 uptake.

ISOTOPE SCAN:-

It detects physiologically active thyroid tissue. Istopes used are ^{123} I ^{131}I and 99m- Technetium pertechnetate. According to uptake nodules are classified as

Cold - No detectable uptake

Warm - Normal uptake

Hot - Increased uptake

The risk of malignancy is 15 to 20% in cold lesions and 5% in warm nodules.

I 131 – half life 8 to 10 days and used to screen and treat patients with differentiated thyroid cancers for metastatic disease.

FNAC:-

It was first reported by martin and Ellis at sloan kettering cancer institute in 1930.

Advantages:-

- ❖ Out patient procedure
- ❖ No anesthesia
- ❖ Cost effective
- ❖ Low complication rate

COMPLICATIONS:-

Local hemorrhage – dissipates spontaneously

Tracheal puncture - coughing - spontaneous recovery

According to FNAC report, patients were classified in 3 groups as per EDDIS Classification (1981)

The utility of FNAC depends on the experience of pathologist to specify and predict neoplasia to rule out malignancy. It is relatively cost effective procedure and has gained patient acceptance.

FNAC can confirm the diagnosis of most primary cancer like papillary, medullary and Anaplastic thyroid cases as well as lymphomas. But follicular and hurthlecell carcinomas cannot be differentiated from from benign counterparts by cytology it requires histological evidence of vascular or capsular invasion

SATISFACTORY SMEAR:-

6 clusters of benign cells in atleast 2 slides prepared from separate aspirates is the minimum material needed to diagnose benign lesion.

ULTRA SOUND GUIDED FINE NEEDLE ASPIRATION (US-FNA) :-

Recently ultrasound guided FNAC has become popular because of increased precision and the ability to guide the biopsy needle to the desired location in real time.

Indications (8)

1. Non diagnostic results by palpation guided FNAC

2. Complex (Solid /Cystic) nodule
3. Palpable small nodule <1.5cm
4. Impalpable incidentaloma
5. Abnormal cervical nodes
6. Nodule with suspicious ultrasonographic features.

Recent studied show that US-FNA decreases non diagnostic rates from 15% to between 3.5% to 7%

ULTRASOUND PREDICTION OF MALIGNANCY (8)

Although no single ultrasound characteristic can unequivocally distinguish benign and malignant nodules, several features and more importantly a combination of features, have been evaluated as predictors of malignancy.

ULTRA SOUND FEATURES OF MASLIGNANCY:-

- Microcalcifications – small intra nodular punctate hyperechoeic spots with scanty or no posterior acoustic shadowing.
- Irregular or indistinct nodule margins
- Chaotic appearance of intra nodular vascular image
- Hypoechoeic appearance of the nodule
- Nodule shape rounded appearance or a “more tall (antero posterior) than wide” shape of the nodule
- Suspected cervical Lymph adenopathy

TECHNIQUE:-

Ultrasound machines with 7.5 to 10MHZ transducers give clear, concise and continuous visualization of the thyroid gland and permit real time visualization of the needle tip during FNA procedure to ensure accurate sampling of the desired area.

After the biopsy sites are identified, the needle is inserted just above the centre of the transducer. Because of the direct visualization of the needle , injury to vital neck structures is easily avoided. The needle should be directed to the peripheral part rather than central part to avoid cystic degenerative areas in nodule center. In case of pure cyst, the center of the lesion should be reached first to completely drain the fluid and submitted for cytologic analysis

In mixed lesion, the needle should be directed to the root of hubs or pedicles growing into cystic lumen (the inner area of the pedicle facing the lumen usually contains necrotic debris and cells with degenerative changes) After complete drainage of the fluid , the solid areas and the peripheral borders of the lesion should be carefully sampled. FNAC features of various thyroid disorders are described in the following section

NODULAR COLLOID GOITER

CRITERIA FOR DIAGNOSIS:-

- Abundant colloid
- Small to moderate number of follicular epithelial cells in monolayer sheets or poorly cohesive groups.
- Fragile cytoplasm, many bare nuclei
- Differential diagnosis: - Inadequate samples, follicular carcinoma
  cystic papillary carcinoma.

AUTO IMMUNE THYROIDITIS

CRITERIA FOR DIAGNOSIS

CLASSIC TYPE

- ❖ Oxyphylic transformation of epithelial cells (Askanazy cells)
- ❖ Scanty or no colloid
- ❖ Moderate numbers of lymphocytes and plasma cells.

FLORID TYPE :-

- ❖ Mixed population of numerous lymphocytes as in reactive lymphadenits
- ❖ No colloid
- ❖ Scanty or normal epithelium

Differential diagnosis ; lymphoma

FOLLICULAR NEOPLASM:-

Criteria for diagnosis

- ❖ Cellular often bloody smear
- ❖ Epithelial clusters of equal size scattered throughout the smear
- ❖ Syncytial cell aggregates with nuclear crowding
- ❖ Microfollicles, rosettes
- ❖ Scanty/ absent colloid

Findings are similar in follicular adenoma and carcinoma. Both are cellular composed of syncytial clusters of cells. There is a tendency for uniform nuclear arrangement in malignant nodule. Anisokaryosis is common in benign lesion.

PAPILLARY CARCINOMA

- Syncytial aggregates with nuclear crowding
- Enlarged pale nuclei ovoid, powdery chromatin
- Multiple distinct nucleoli
- Intra nuclear cytoplasmic inclusions, nuclear grooves
- Dense cytoplasm
- Psammoma bodies

MEDULLARY CARCINOMA:-

- Cellular smears with dispersed cells
- Variable cell pattern plamacytoid, small spindle cell
- Uniform stippled chromatin
- Amyloid back ground (pink)
- Calcitonin positive staining

ANAPLASTIC CARCINOMA:-

- Bizarre, large, malignant cells epithelial /spindle Sarcomatoid type
- Prominent nuclear pleomorphism
- Mitotic figures
- Giant cell and spindle cell variants

AFTER FNAC, CASES CAN BE CLASSIFIED INTO :-

- Benign 65%
- Suspicious 20%
- Malignant 5%
- Non diagnostic 10%

Incidence of false positive rate is approximately 1%

False negative report is approximately 3%

BENIGN:-

- Nodular goiter
- Colloidgoitre
- Lymphocytic thyroiditis
- Simple cyst
- Colloid nodule

SUSPICIOUS:-

- Hurthle cell lesion
- Follicular cell lesion

MALIGNANT:-

Papillary, medullary, Anaplastic, lymphoma

NON DIAGNOSTIC: -

Suggested repeat FNAC

IMMUNE HISTOCHEMICAL MARKERS:-

Several molecular markers are used to clarify suspicions FNAC result. HMBE-1 is a mono clonal antibody that stains papillary carcinoma but does not stain benign follicular tumors. Galectin-3 which act as cell death suppressor is used to distinguish benign and malignant thyroid follicular tumors. But their sensitivity and specificity are low.

HISTOPATHOLOGY

The specimens are given unique number and submitted for macroscopic assessment. They are left in formalin for atleast 1 day. A written description made. Representative samples are taken. Colored inks are used to identify surfaces.

Samples are placed in cassettes and embedded in paraffin wax to make a block. Sections with 5μm thickness are cut from the block using microtome. Sections are placed on glass slides and stained with haematoxylin and eosin (H and E). The slides are examined with a microscope by histopathologist and report given.

Microscopically the normal thyroid gland is made of round or oval follicles with an average diameter of 200μm. They are lined by single layer of follicular cells whose shape ranges from flattened to low columnar depending on their degree of activity.

The cytoplasm has a acidophilic staining quality: the greater the activity of the cell the greater the amount. The proliferative activity of follicular cells is related to age being highest in the prenatal group and lowest in adults.

The main ultra structural features of follicular cells are abundant granular endoplasmic reticulum, well developed golgiapparatus, Lysosomes and numerous microvillus in the luminal border. The intra luminal colloid is pale staining with scalloped borders in follicles with active secretory function and densely eosinophilic in inactive ones.

Immunohistochemically, reactivity for thyroglobulin is found both in the colloid and cytoplasm of the follicular cells.

Thyroid transcription factor I(TTF-1) is another important tumor marker for follicular cells.

The other major epithelial component of the thyroid gland is represented by neuroendocrine cells known as C'cells or para follicular cells.

The name parafolliculor cells is a misnomer, because immunohistochemical and ultrastructural studies have shown that they occupy exclusively intrafollicular position.

Since they arise from neural crest via ultimo bronchial body they are restricted to middle and upper thirds of the lateral lobes along their central axes.

The number of c cells varies according to age: they are numerous in infancy and old age then in adults. Most adult glands contain no more than 10 c cells in low power microscopic field. Ultrastructurally, c cells contain numerous dense core granules of neurosecretrory type solid cell nests (rests) measuring 0.1mm on average can be detected in almost 90% neonatal thyroid gland they represent remnants of ultimobranchial body.

MORPHOLOGIC VARIATIONS HAVING NO CLINICAL SIGNIFICANCE INCLUDE:

1. Adipose metaplasia of Interfolliculor stroma
2. Intrathyroidal islands of mature cartilage, presumably of bronchial pouch derivation.
3. Intrathyroidal islands of ectopic thymus
4. Intrathyroidal parathyroid.
5. Intrathyroidal bundles of skeletal muscle
6. Intrathyroidal salivary gland tissue
7. Accumulation of melanin –like pigment in the cytoplasm of follicular cells in old age that may become massive after administration of minocycline. It is called as melanosis thyroidi or black thyroid.

HETEROTOPIC THYROID TISSUE

Heterotopic thyroid tissue can be found not only as a component of thyroglossal duct cyst but any where along the course of the thyro glossal duct. The most frequent location is base of tongue

The heterotopic thyroid does not differ microscopically from that seen in the main gland. sometimes a capsule is formed around it in other instances, the follicles grow between the skeletal muscle of the tongue, a feature that may simulate invasion by tumor.

Other sites of heterotopic thyroid tissue are the anterior tongue, submandibular region, larynx, trachea, superior mediastinum and heart.

The common denominator in all these sites is their location in or close to midline. That area is called as wolfer's area and isosceles triangle by anatomists. The edge of the mandible forms the base and concavity of the aortic arch forms its apex.

Other rare sites include porta hepatis , adrenal gland and ovary.

Heterotopic thyroid tissue in any of these locations can be affected by the same disease that affects main gland (inflammation, hyperplasia, tumor)

DYS HORMONOGENETIC GOITER :-

There are several types of goiter resulting from enzyme defects in hormone synthesis.

Grossly the gland is enlarged and multinodular.

Microscopically hyper cellular nodules exhibiting a variety of architectural appearances with predominance of solid and microfollicular patterns. Fibrosis may be seen.

A diagnostically important feature is the nuclear atypia (in the form of bizarre hyperchromatic nuclei) is present mainly in tissue between the hyperplasic nodules rather than in the nodules themselves.

As a result of continuous thyrotropin stimulation mitotic figures are seen.

GRAVES' DISEASE (DIFFUSE TOXIC GOITER)

Usually presents in young adult female. Grossly the gland shows a mild to moderate symmetric diffuse enlargement. It is succulent and reddish and has the consistency of pancreatic tissue. The cut surface is uniformly gray or red depending on the degree of vascularity.

Microscopically the follicles are hyperplasic with prominent papillary infolding that may cause confusion with papillary carcinoma.

The colloid is pale and finely vacuolated with prominent scalloping where it abuts the epithelium.

The stroma contains lymphoid tissue aggregates with germinal centre formation.

NODULAR HYPERPLASIA – (MULTINODULAR GOITRE, SOLITARY NODULAR GOITRE, ADENOMATOUS HYPERPLASIA)

Nodular hyperplasia is the most common thyroid disease.

Grossly, the thyroid is enlarged, its shape distorted the thyroid capsule may be stretched but is intact

On cross section, multiple nodules are seen, some surrounded by a partial or complete capsule. Secondary changes in the form of hemorrhage calcification and cystic degeneration are common

Microscopically there is a wide range of appearances some nodules may have huge follicles lined by flattened epithelium, some may be extremely cellular and hyperplastic and some may be composed of hurthle cells.

Huge dilated follicles may have a group of small active follicles at one pole called as Sanderson's polsters

There may be papillary projections protruding towards the centre of a cystically dilated follicle. This particular feature may lead to confusion with papillary carcinoma.

When follicles rupture, the exposed colloid induces granulomatous reaction with the appearance of histiocytes and foreign body type of giant cells.

Areas of fresh and old hemorrhage, coarse fibrous trabaculation and foci of calcification are common.

Variable number of chronic inflammatory cells are present in the stroma; the larger their number the higher the chances of post operative hypothyroidism.

The presence of atypical nuclei in case of nodular hyperplasia should raise the possibility of previous exposure to radioactive substances.

The differential diagnosis between a dominant nodule from a case of nodular hyperplasia and a true adenoma is based on a set of arbitrary criteria.

The adenoma is usually single, is totally surrounded by a capsule, is dissimilar from the remaining parenchyma, compresses adjacent tissue and is composed mainly of follicles that are smaller than those of the normal gland.

The lesion of nodular hyperplasia is almost always one of the many nodules, its capsule is incomplete, the follicular size is variable, and there is no compression of adjacent parenchyma.

Hashimoto's thyroiditis

It is predominantly a disease of women over 40yrs of age.

Grossly, the typical case shows diffuse enlargement of the gland. However in some cases one lobe is more enlarged than the other and in others the disease has a distinctly multinodular quality. The consistency is firm but not stony hard as in riedel's thyroiditis .

The cut surface is friable, vaguely nodular, yellowish gray and resembles hyperplasic lymphnode. Necrosis and calcification are absent. Colloid is not clearly discernible

Microscopically, the following feature are seen.

1. Lymphocytic infiltration of the stroma

2. Oxyphilic change of the follicular epithelium.
3. Lymphoid tissue exhibits large follicles with prominent germinal centres.
4. Plasma cells, histiocytes and giant cells can be present
5. Variants fibrous and juvenile type

The thyroid follicles are small and atrophic. Most of them are lined by variable sized hurthle cells.

Immune histo chemically, the follicular cells of autoimmune thyroiditis resemble papillary carcinoma by showing greater reactivity for keratin, s-100 protein HLA-DR In typical case of Hashimoto's the connective tissue is scanty. But in fibrous variant –fibrosis is more extensive.

In contrast to riedel's this is of dense hyaline type and does not extend beyond the thyroid capsule.

Complications of hashimoto's include malignant Lymphoma leukemia, papillary carcinoma and Hurthle cell neoplasm. Because all these there conditions evolve gradually from a setting of hyperplasia of the respective cell component, their early identification may be extremely difficult.

RIEDEL'S THYROIDITIS

- Grossly the process is asymmetric and involves only localized areas of the gland.
- The affected portion is stony hard and cuts with great resistance.
- Dense fibrous tracts extend from the thyroid capsule into adjacent muscle resulting in obliteration of tissue planes during surgery.
- Microscopically the following features are seen
  - Extensive fibrous tissue completely replacing the involved area of gland.
  - Skeletal muscle cells in immediate area are directly infiltrated by fibrous tissue.

Follicular Adenoma

It is a benign encapsulated tumor that shows evidence of follicular cell differentiation.

Adenomas are almost solitary except in genetically determined syndromes like cowden syndrome.

Grossly adenomas are characteristically surrounded by thin capsule.

Variants -	Normo follicular	-	Simple
	Macro follicular	-	Colloid
	Micro follicular	-	Fetal
	Trabacular	-	Embryonal

Secondary changes like hemorrhage, fibrosis, calcification, bone formation and cystic degeneration are common.

Differential diagnosis includes Hyperplastic nodules and encapsulated papillary carcinoma.

HURTHLE CELL TUMORS :-

These tumors are composed exclusively of follicular cells exhibiting onocytic features.

Mitochondrial accumulation in cytoplasm gives the granular appearance in oncocytes. Grossly, they are solid, tan and encapsulated.

Microscpically the pattern may be follicular, trabacular, or papillary. Follicular pattern is the most common variety. Tumors with capsular and vascular invasion are designated as carcinomas.

The pattern may be follicular, trabacular

Tumor with clear cut capsular and vascular involvement are designated as carcinomas.

PAPILLARY CARCINOMA :-

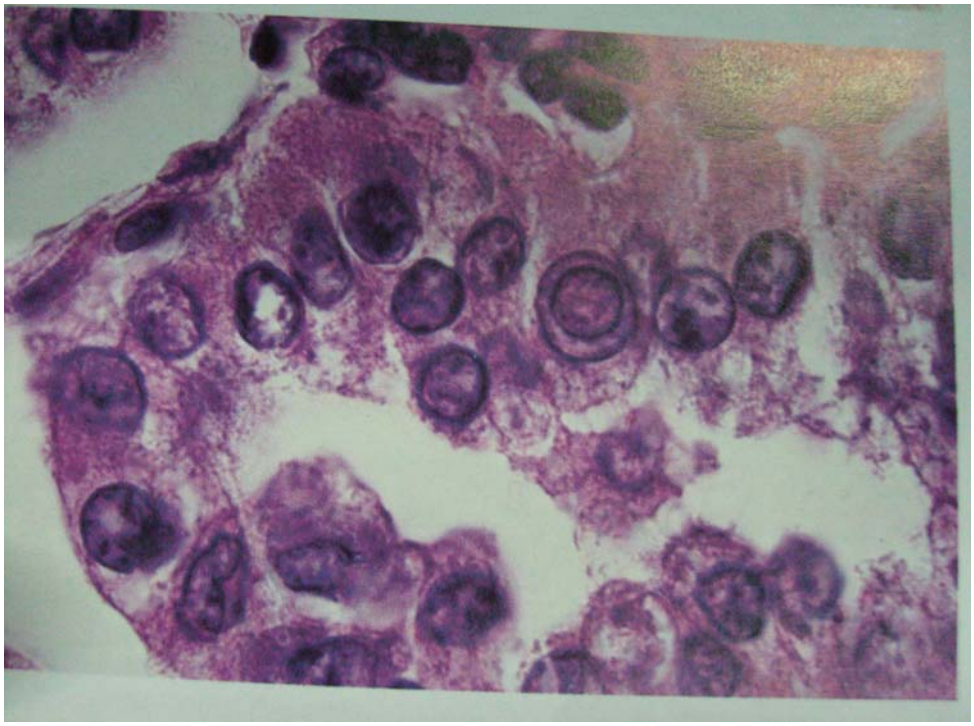
On gross examination, papillary thyroid carcinomas are generally hard and whitish and remain flat on sectioning with blade in contrast to normal tissue on benign nodular lesions that tend to bulge.

Calcification, necrosis or cystic change may be seen.

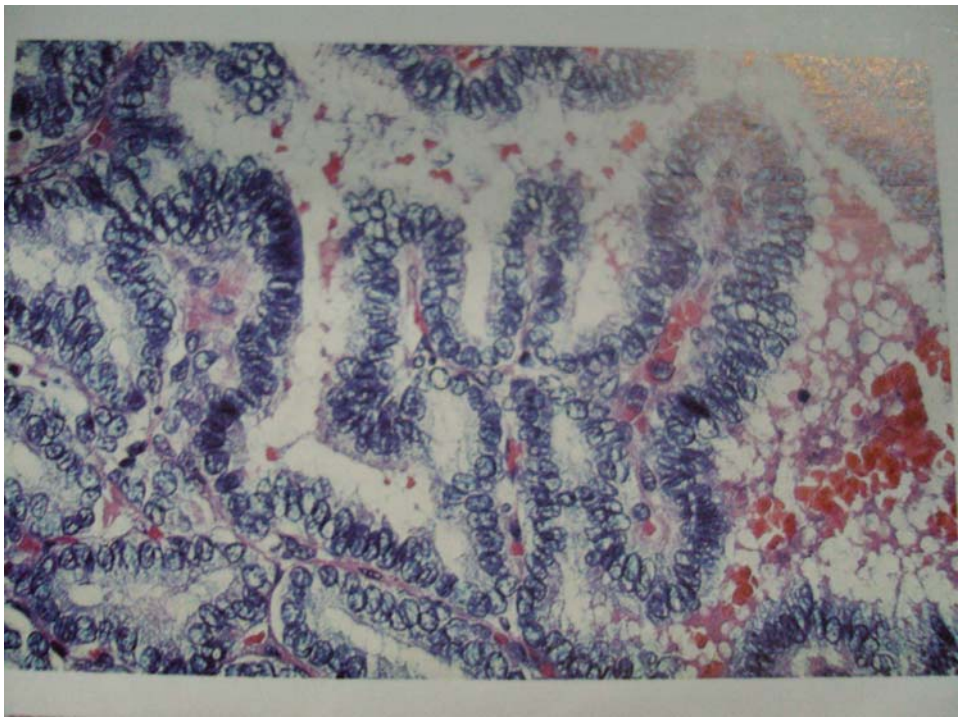
Diagnosis depends on the presence of papillae and nuclear features

1. Ground Glass nuclei with inconspicuous nucleolus pushed against nuclear membrane
2. Nuclear pseudo inclusions
3. Nuclear groove
4. Nuclear microfilaments
5. Psammoma bodies seen in approximately half of the cases

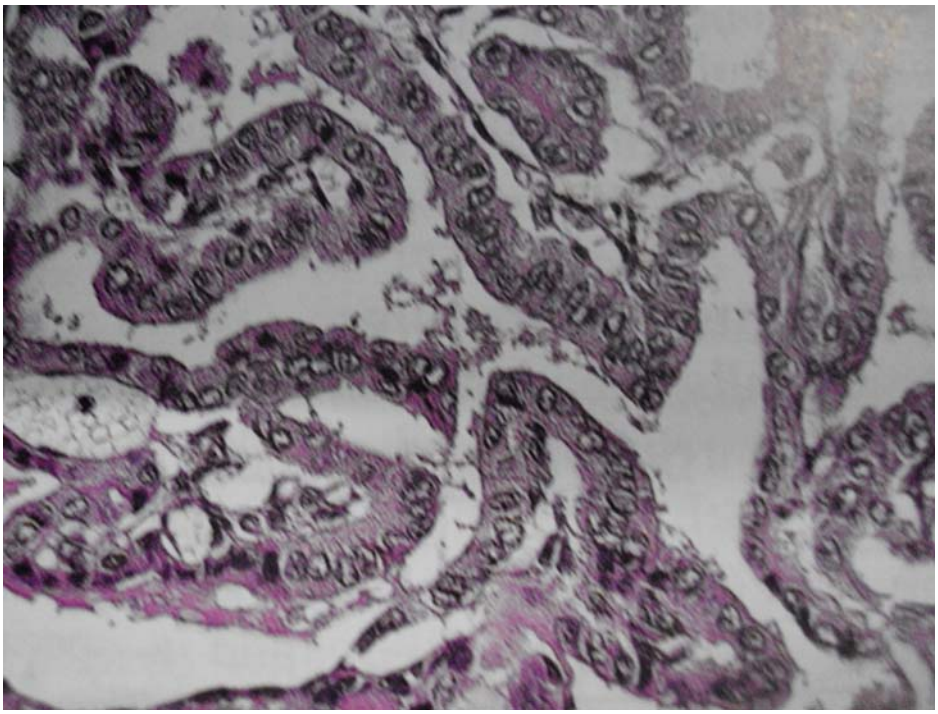
   Psammoma bodies are microscopic calcified deposits representing clumps of sloughed cells.



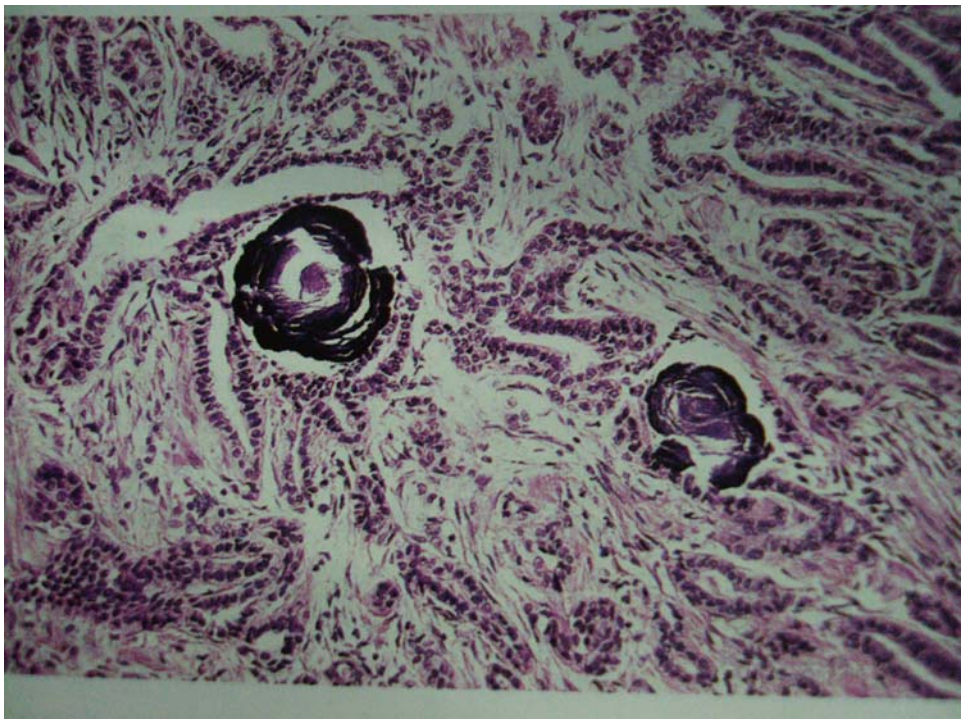
Papillary Carcinoma



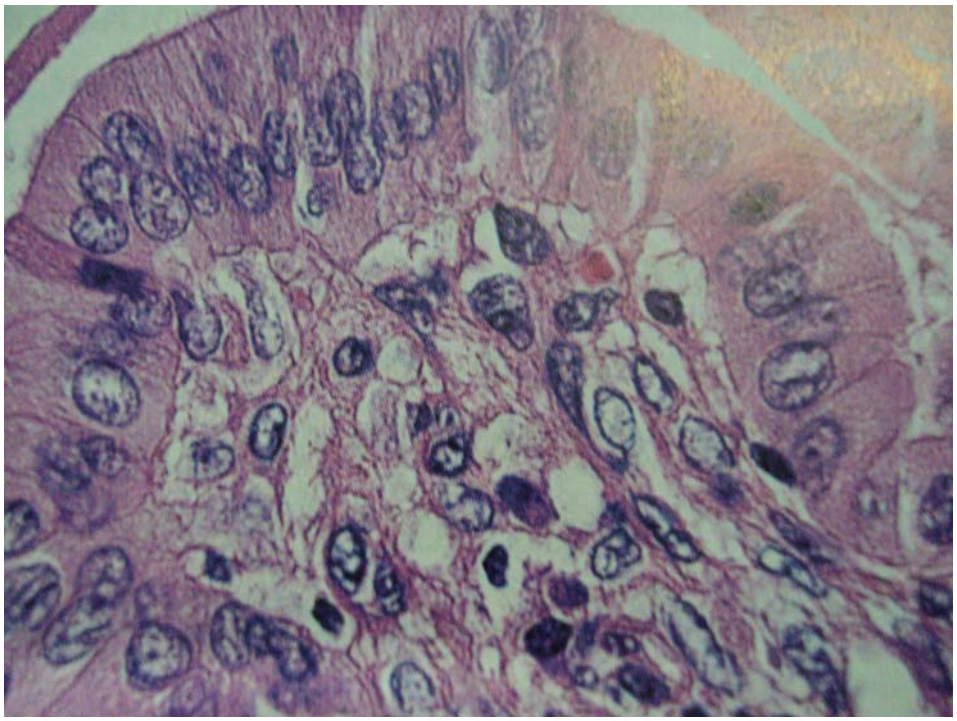
Papillary Carcinoma - Nuclear Pseudo inclusions



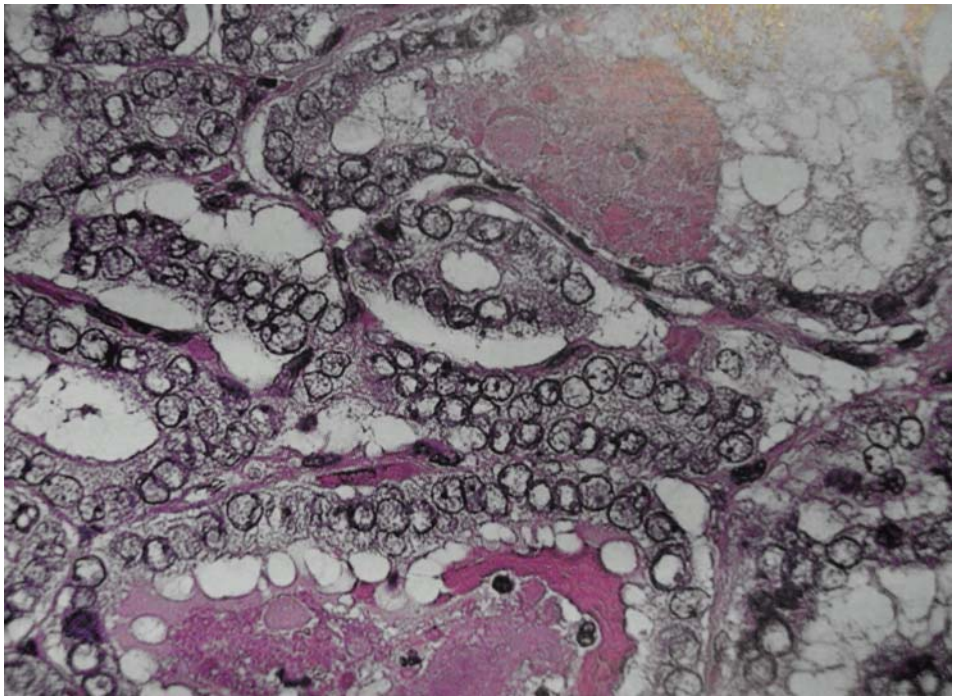
Papillary Carcinoma - Classic Type



Psammoma body - Papillary Carcinoma



Tall Cell Variant - Papillary Carcinoma



Follicular variant - Papillary Carcinoma

VARIANTS :-

1. Papillary micro carcinoma
2. Encapsulated variant
3. Follicular variant
4. Encapsulated follicular variant
5. Diffuse sclerosing
6. Oxyphilic variant
7. Tall cell variant
8. Columnar cell variant
9. Clear cell
10. Insular
11. Trabacular

Tall cell, Insular, Columnar, diffuse sclerosing, clear cell, trabacular - variants account for approximately 1% of all papillary tumors are generally associated with worse prognosis.

Occult or micro carcinomas are defined as tumors of 1cm or less in size with no evidence of local invasiveness through the thyroid capsule or angioinvasion and are not associated with lymph node metastases. They are usually incidental findings at operative or histologic examination.

Follicular variant of papillary carcinoma

This is a papillary carcinoma composed entirely of follicles. The diagnosis is based on nuclear features of papillary carcinoma. The follicular variant can be viewed as the balanced result of two biologic properties of the tumor cell; differentiation in the form of secretory activity and proliferation when one of these predominates over the other two further variants emerge.

When proliferation predominates solid variant occurs. Whose behavior is similar to papillary carcinoma.

When secretory activity predominates macro follicular variant is formed. This type resembles hyperplastic nodule.

Follicular Carcinoma

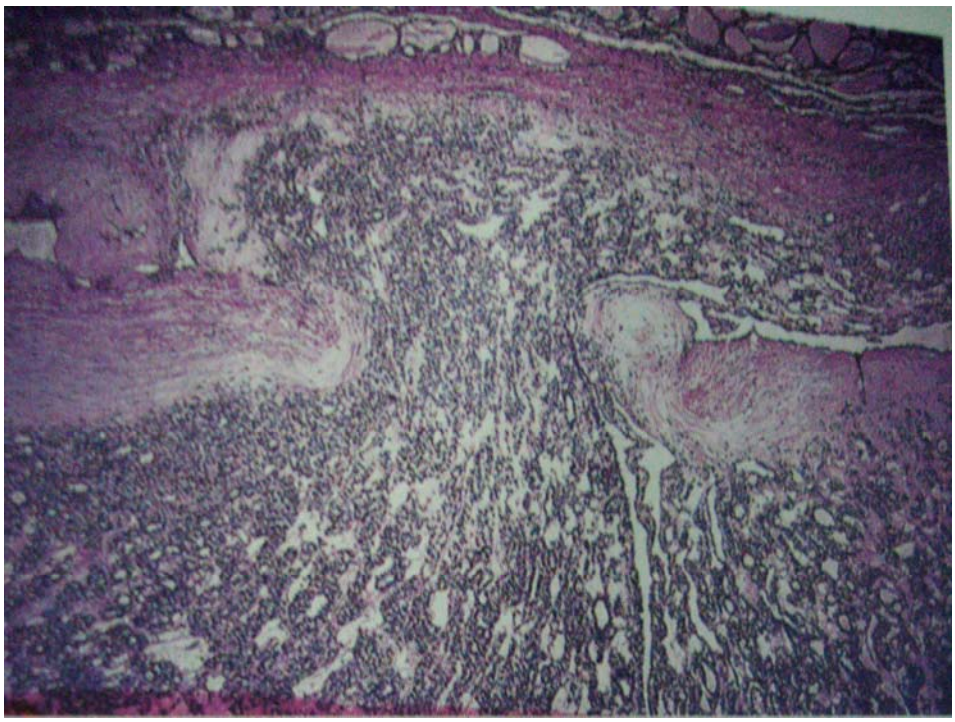
1) Minimally invasive follicular carcinoma:- Grossly encapsulated with solid and fleshy cut surface. Blood vessel and capsular invasion.
2) Widely invasive follicular carcinoma:- lacks capsule, wide spread infiltration of blood vessels and adjacent thyroid tissue.

Microscopically the vessels should be of venous caliber, located in or immediately outside the capsule rather than within the tumor. These vessels lack elastic muscular layer.

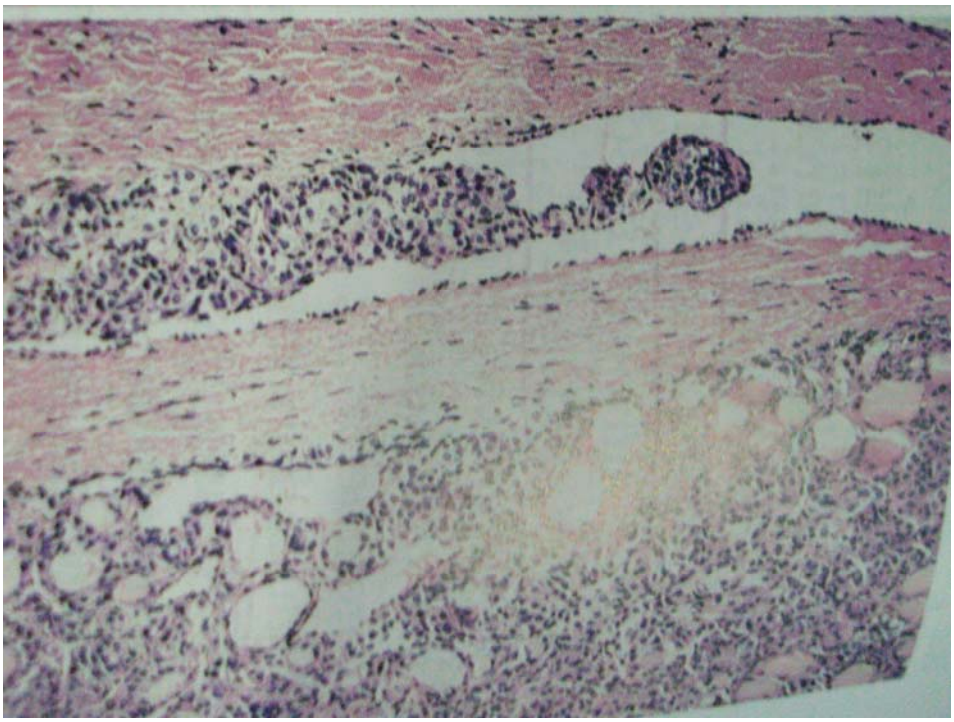
Endothelial markers CD 31, factor VIII related antigen and ulex europaeus is useful.

Interruption of the capsule must be full thickness for the process to qualify as capsular invasion.

When less than 4 blood vessels are involved it is limited vascular invasion type and if more than or equal to 4 vessels involved it is extensive vascular invasion type.



Capsular invasion - Follicular Carcinoma



Vascular invasion - Follicular Carcinoma

MEDULLARY CARCINOMA :-

They may be sporadic or familial. They are typically unilateral in sporadic cases and bilateral in familial forms. Familial form is invariably accompanied by ‘c’ cell hyperplasia.

In the residual gland ‘C’ cell hyperplasia is located in the central part of lateral lobes. The arbitrary figure of more than 6 cells per thyroid follicle has been suggested as an indicator of ‘C’ cell hyperplasia. ON GROSS EXAMINATION they are firm and whitish in appearance.

Microscopically the following features are seen in histopathological Examination

1. Round or polygonal or spindle shaped tumour cells
2. Nuclei tend to be eccentric with coarsely clumped chromatin
3. Amyloid deposits in 80% of cases

VARIANTS :

- Follicular variant
- Papillary variant
- Smallcell variant
- Giant cell variant
- Oncocytic variant

In immuno histo chemistry the calcitonin is the important tumor marker in diagnostic point of view.These tumors also stain positively for CEA and Calcitonin gene related peptide.

ANAPLASTIC CARCINOMA

Usually present is elderly patients as a rapidly growing mass Grossly the tumor is solid with areas of hemorrhage and necrosis.

Microscopically the term undifferentiated or anaplastic carcinoma is used in thyroid gland in connection with two major categories that sometimes coexist. .

The first is undifferentiated in the sense that it does not make follicles, papillae but still retains and unmistakable epithelial appearance on morphologic and immuno histochemical grounds. This pattern is referred as squamoid type with clear cut foci of keratinization.

The second category is composed of two patterns which are often seen together and grouped as sarcomatoid type spindle cell and giant cell

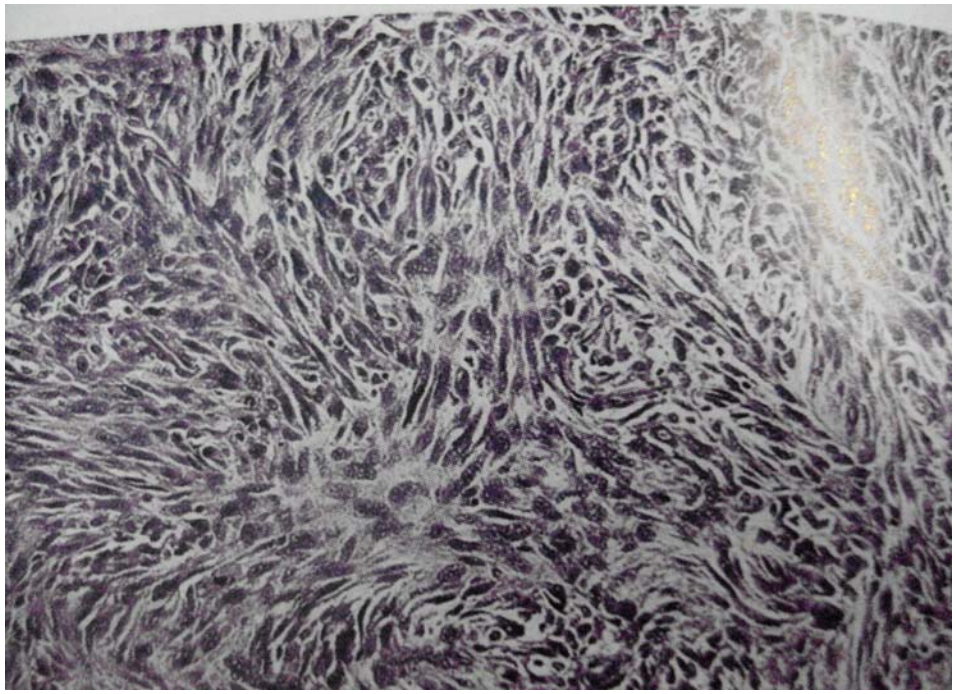
There are two variants

Spindle cell and giant cell patterns

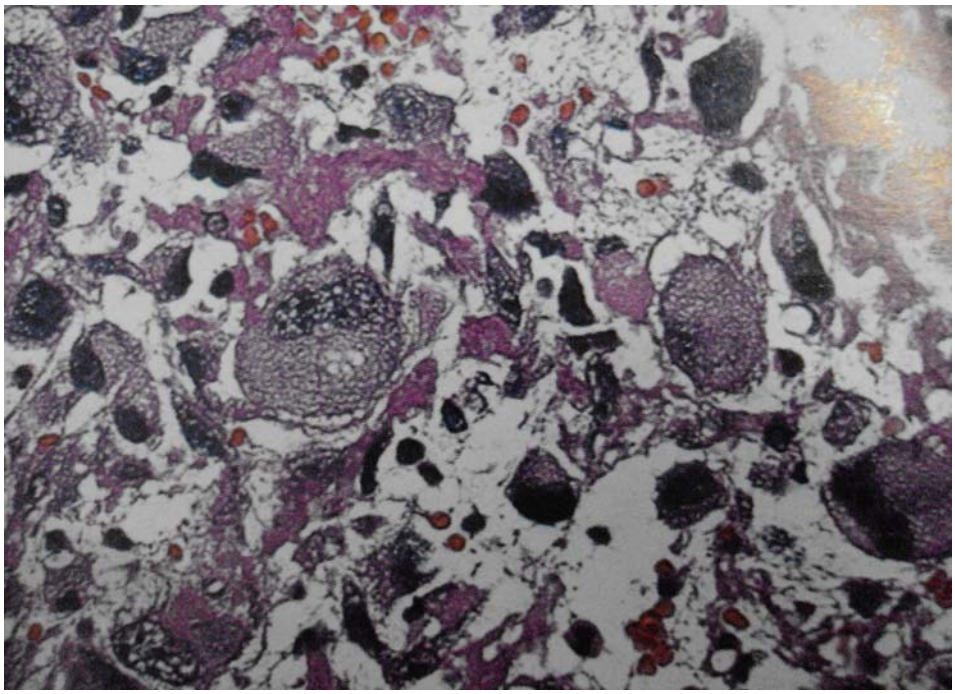
Cellular pleomorphism

High mitotic activity, necrosis

Invasion into gland and adjacent structures



Anaplastic Carcinoma - Spindle Cell Type



Anaplastic Carcinoma - Giant Cell Type

MATERIALS AND METHODS

MATERIALS AND METHODS

This study include the patients who were operated for solitary and multinodular thyroid disease, suspicious malignant disease and malignant disease.

All cases were studied in detail with detailed clinical examination and investigations. Cases with hard thyroid swelling, male sex, fixity to surrounding structures, nerve involvement and cold nodules are studied in detail to rule out malignancy. Cases with cystic swellings are not aspirated they were subjected to surgery to rule out papillary carcinoma.

Study period :-

In our study the study period is between July 2008 to September 2009.

Study site:

General surgery department, Kilpauk, Medical College, Pathology department Kilpauk Medical College,

Study design:-

Prospective study.

Equipments for FNAC:-

FNA gun or 10cc syringe

22 to 24 gauze needle

Syringe holder

Glass slides

Alcohol

Fixative

Gauze pad

Adhesive bandage

PROCEDURE:-

Initial examination should be with patient in upright position but FNAC done in supine position. Place a pillow under the neck. Ask the patient to keep still and to refrain from swallowing. Perform 2 to 4 aspiration in same session.

Depending on the size of the thyroid swelling use different angles and change in point of entry. Cells are placed and prelabelled in dry glass slides. Some are immediately placed in 70% alcohol while others are air dried.

The stain used is papanicolaou or wrights stain. Skilled pathologist can accurately diagnose thyroid lesions.

GROUP I BENIGN

All patients whose clinical examination showed features of solitary or multinodal thyroid disease with preoperative FANC as nodule, colloid, adenomatous goitre.

GROUP II SUSPICIOUS MALIGNANCY

Solitary nodular or multinodular goiter with pre operative FNAC showing follicular neoplasm.

GROUP III

- Hard swelling
- Pre operative FNAC showing malignancy
- H/o recent voice change
- H/o difficulty in breathing or swallowing
- Fixity to surrounding structures.
- Lymph node enlargement (secondary from thyroid nodule)

ALL 100 PATIENTS UNDERWENT SURGERY**. FINAL**

HISTOPATHOLOGY REPORT OBTAINED FOR ALL PATIENTS.

RESULTS AND ANALYSIS

RESULTS

In our study out of 100 patients 11 were male and 89 were female patients Solitary thyroid Nodule observed in 36 cases (Male 7 - Female 29) Multinodular goiter observed in 64 cases (Male -4 Female 60).

SEX INCIDENCE

Male -11 cases.

Female -89 cases.

AGE INCIDENCE

Nodular thyroid disease occurred in age group of 10 to 70yrs.

Youngest patient 16 yrs.

Oldest patient 67 yrs.

Maximum incidence of 13 cases of solitary Nodular goiter recorded in 21to 30 yrs age group.

Maximum incidence of 21 cases Multi Nodular goiter recorded in 30 to 40 yrs age group.

INCIDENCE OF BENIGN AND MALIGNANT LESIONS

In our study as per HPE report

Among 89 female case

- 12 cases are papillary carcinoma
- 2 cases are medullary carcinoma
- 75 cases are benign disorders

- Among11 Male cases
- 3 Case were papillary carcinoma, 8 cases are benign disorders

Percentage of Benign Lesions

Female : 84.3%

In male : 72.7%

Percentage of malignant lesions :-

Female : 15.7%

Male : 27.2%

AMONG SOLITARY NODULAR GOITER: - AS PER FNAC

Nodular colloid goiter -23 cases

Follicular Neoplasm -7 cases

Hurthle cell neoplasm -1 case

Papillary neoplasm – 5 cases

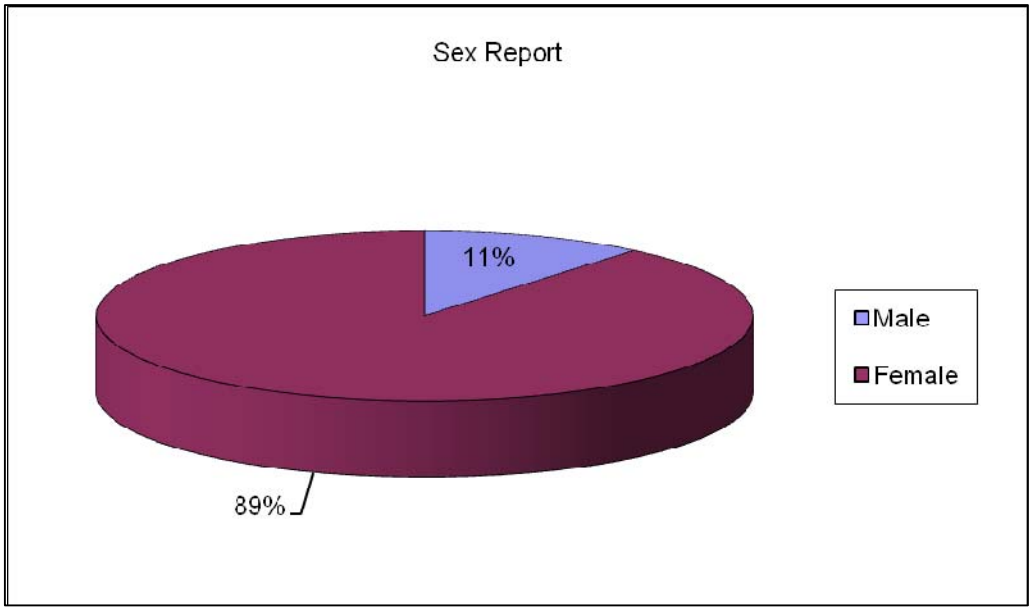
AMONG MULTINODULAR GOITER AS PER FNAC

Nodular Colloid goiter - 59 cases

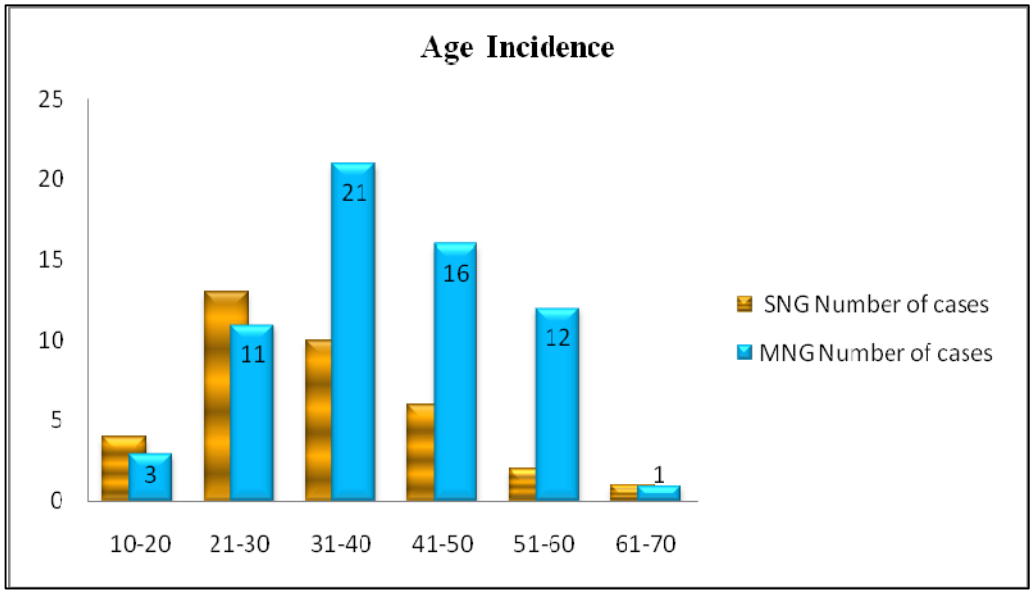
Follicular Neoplasm – 4 cases

Hurthle cell neoplasm – 1 case

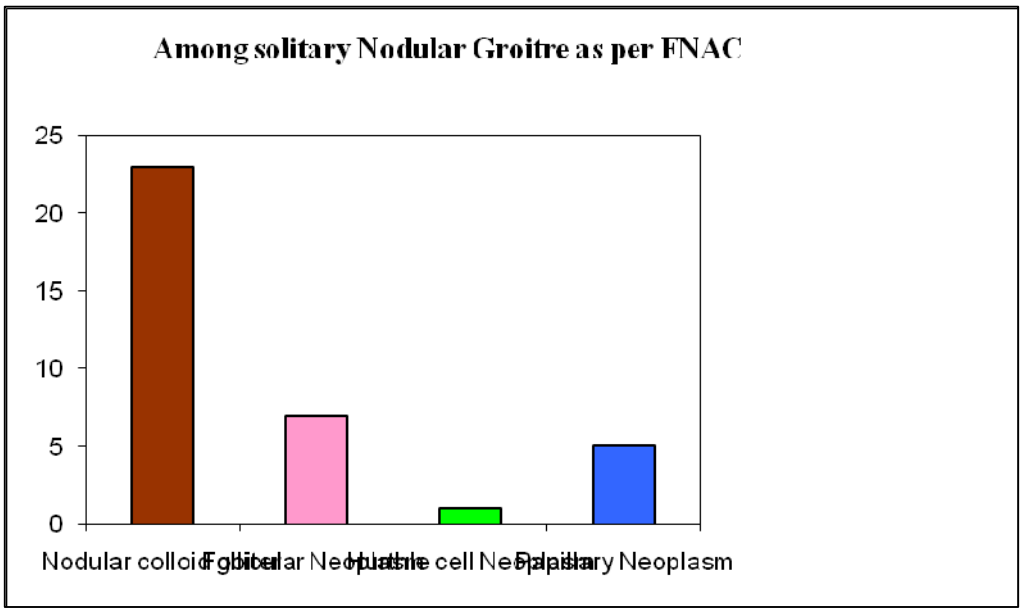
SEX REPORT



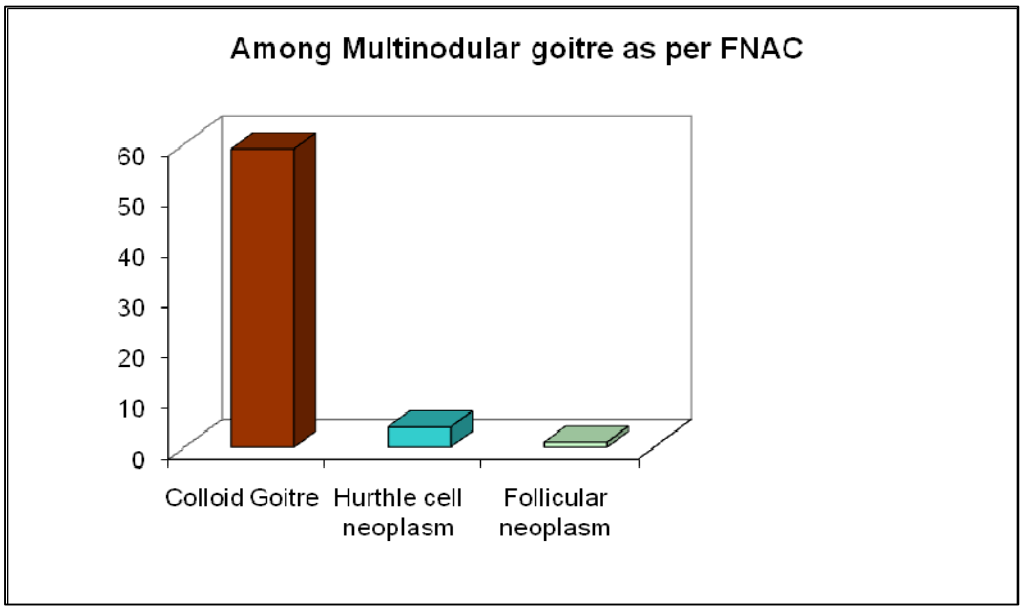
AGE INCIDENCE



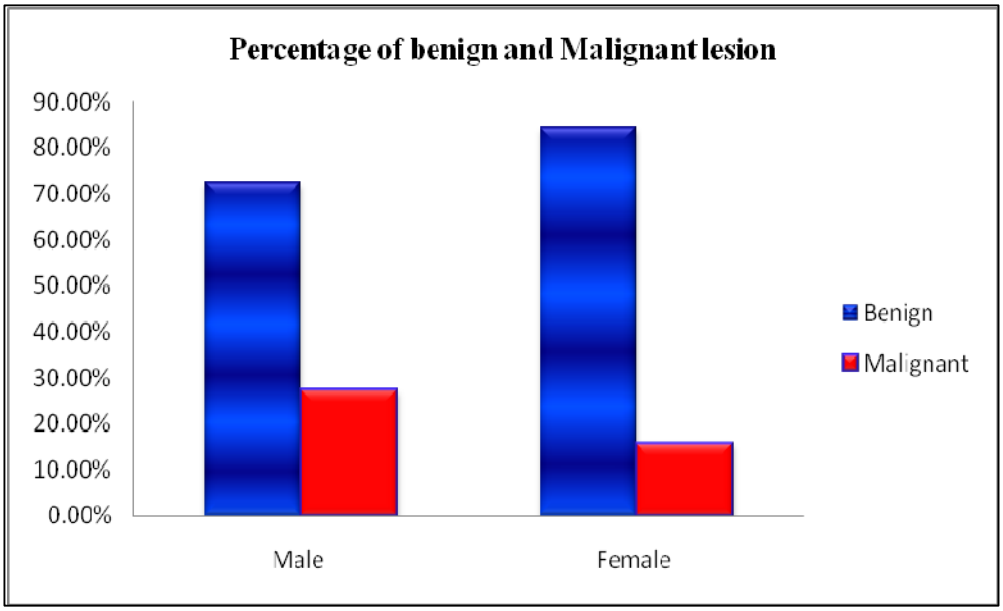
AMONG SOLITARY NODULAR GROITRE AS PER FNAC



AMONG MULTINODULAR GOITRE AS PER FNAC



PERCENTAGE OF BENIGN AND MALIGNANT LESION



GROUP I

Solitary Nodular Goiter

Male - 5

Female - 18

Right Lobe -15

Left Lobe – 8

Number of pre operative FNAC =23

Correlated with HPE = 20

Percentage of correlation = 87%

Discordance in biopsy =3

Percentage of Discordance = 13%

Multi Nodular Goitre

Male = 4 cases

Female = 55 cases

Pre operative FNAC 59 cases

Correlated with Biopsy :39 cases

Percentage of correlation : 66%

Discordance in Biopsy = 20

Percentage of discordance = 34%

Group II

Male -2

Female -11

Among 13 cases

Preoperative FNAC

Correlated with Biopsy -8

Percentage of correlation 61.5%

Discordance in Biopsy:5

Percentage of discordance: 38.5%

Group III

Solitary Nodular Goitre

Female -5

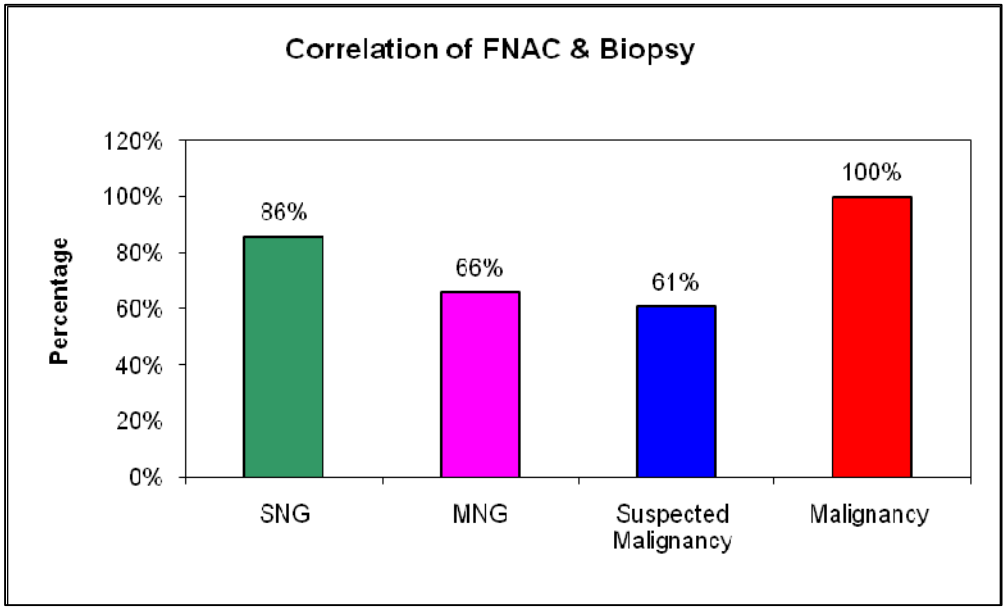
Male – Nil

Correlated with Biospy =5 cases

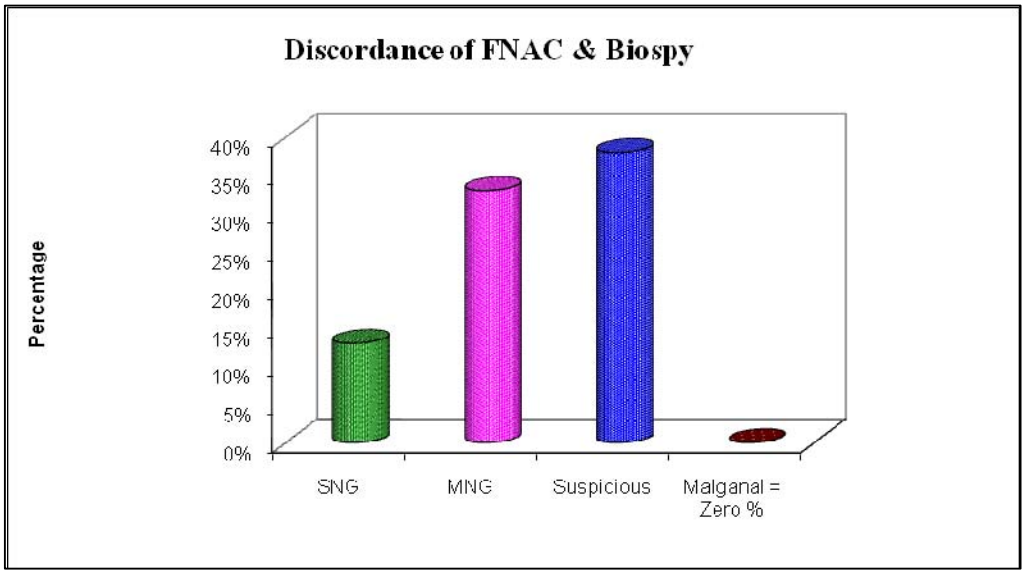
Percentage of correlation – 100%

Percentage of discordance – 0%

CORRELATION OF FNAC & BIOPSY



DISCORDANCE OF FNAC & BIOSPY



DISCUSSION

DISCUSSION

FNAC is easy to perform and safe with minimum complication rate. Care must be taken to obtain an adequate specimen- most authors recommend between 3 to 6 aspirations. Satisfactory specimen contains atleast 6 groups of 10 to 15 well preserved cells. They are categorized by their appearance to benign, indeterminate or suspicious and malignant.

The diagnosis of papillary thyroid carcinoma by FNAC on the basis of characteristic nuclear changes is reliable and accurate with sensitivity and specificity both approaching 100%.

In our study among 100 cases 5 cases are reported as papillary carcinoma in FNAC. But after HPE report 15 cases are diagnosed as papillary carcinoma. Among 15 cases, 5 cases are follicular variant type, and 2 cases are Tall cell variant type. About 10 case of papillary carcinoma are misdiagnosed in FNAC.

In case of follicular neoplasm the sensitivity of FNAC is about 90% and specificity less than 50% this limits the usefulness of FNAC. Tpo immuno chemistry with monoclonal antibody (MO Ab 47) improves the

accuracy of FNAC for follicular lesions. It increases sensitivity to 100% specificity to 70%

B.Mundasad, P.C. pyper 2006 (15) conducted a study on Accuracy of FNAC in diagnosis of thyroid swellings. In their study among 144 patients - FNAC revealed 94% benign, 6% malignant 4% suspicions. 13% inadequate, 4% indeterminate. But histopathology showed 82% benign, 18% malignancy. In their study the inadequate sample rate was 13%. The most important factors include experience of the aspirator and criteria used to define a satisfactory sample. Published dates suggest inadequate sample ranges between 9 to 31% in their study false negative rate is 23% ie FNAC negative for cancer but histology positive for cancer.

As per AACE /AME task farce on thyroid nodules Endocr pract 2006:124 63-102 the average false negative rate is 5% their guidelines to minimize false negative results are. (9)

1. Aspirate multiple nodule sites
2. Aspirate multiple nodule sites in MNG
3. Follow up cytologically benign nodules

4. Submit cyst fluid for examination
5. Review studies with experienced cytopathologist

Oliver H beechars stated that goiters were frequently seen in women however, the incidence of carcinoma in man is greater than in women.

In our study among 100 cases, the incidence of carcinoma in Male ((27.7%) is greater than in female (15.7%). This is in accordance with various published reports.

Fenn,Krishnan 1976 found that there was no great sex predominance in the incidence of malignancy (20).

According to prof R.C suryaprakash – Andhra Pradhesh – Adenoma thyroid was the commonest benign lesion and papillary carcinoma was the commonest malignant lesion.

Prof. R.L Gupta Delhi analyses 370 cases of solitary nodule. In his study, about 38.7%. OF HPE report was different from FNAC. His study showed the fact that FNAC is not fullproof and surgery with HPE report remain the only method of confirmation.

As Per Hossein gharib and papini (8) nodule size is not predictive of malignancy. They have reported the following features are associated with increased risk of malignancy in thyroid nodule

H/o of childhood head and neck radiation

Family H/o of PTC, MTC, or MEN 2 (multiple endo crine neoplasia)

Age 20 or >70 yrs

Male sex

Abnormal cervical adenopathy

Fixed nodule

Vocal cord paralysis.

They concluded that risk of cancer is not significantly higher for solitary nodular than for glands with multiple nodules.

But in our study the incidence of carcinoma in solitary nodular goiter (22.2%) is more than multinodular goiter (10.9%)

As per feld while the prevalence of thyroid nodule is les common in children, the risk of malignancy appears to be much higher 14 to 40% as apposed to 5% in adults

According to koh and cole WH, the incidence of carcinoma in MNG varies from 7% to 17% (14).

In our study the incidence of carcinoma in MNG is 10.9%

Pier paolo gandolfi,(13) antoniofrisina Italy conducted retrospective study among 58 cases who were operated for MNG. In their study, the incidence of carcinoma is 13.7%. They have stated that risk of malignancy should not be under estimated and a dominate nodule in MNG should be valued as it were a single nodule in an otherwise normal gland.

Raghuveer pedamullu katuri medical college conducted retrospective study of 98 cases of MNG who underwent total thyroidectomy at guntur government general hospital (India) from 2001 to 2004 he found the prevalence of MNG in female 88% in males 12% and incidence of female 88%.

He concluded that inspite of negative FNAC the patients can still harbor a malignant focus due to high sampling error with MNG.

Ghasal analyzed 75 patients with solitary nodule accurate correlation of FNAC HPE and report was possible only in 55 cases. (22).

In our study among 36 solitary nodular goiters FNAC and HPE report correlation was possible only in 27 cases.

Gita Jayaram of New Delhi 1984 condoled FNAC study in 308 cases of SNG. She also pointed out difficulty in diagnosing follicular neoplasm and more number of false negative reports (23).

Kelly Lester lay field reported the evaluation of cold nodule is a problem. It needs HPE for further management. (19)

CONCLUSION

CONCLUSION

- In our study the commonest thyroid disease affecting study population are solitary nodular goiter, multinodular goiter, hashimoto's, papillary carcinoma thyroid.

- The percentage of correlation in Group I Solitary Nodular Goitre 87% and Multinodular goiter 66%

- The percentage of discordance in Group I Solitary Nodular Goitre 13% Multinodular goiter 34%

- The percentage of correlation in Group II 61.5%

- The percentage of discordance in Group II 38.5%

- The percentage of correlation in Group III 100%

- The percentage of discordance in Group III is 0%

- This study concludes nodular colloid goiter is the commonest benign lesion and papillary carcinoma is the commonest malignant lesion.

- The incidence of malignancy in Multinodular goiter10.9%

- Incidence of carcinoma in solitary nodular goiter 22.2%

- FNAC is simple, safe, and cost effective but HPE remains final diagnostic tool. Because FNAC cannot differentiate between adenoma and carcinoma in follicular and hurthle cell lesions.

- For example in our study 10 cases were reported as follicular neoplasm in FNAC. Among them 6 cases were follicular adenoma, 3 cases were papillary carcinoma (follicular variant type) and one case medullary carcinoma in HPE report.

- In our study 2 cases were suspected as Hurthle cell neoplasm in FNAC. After surgery one case became hurthle cell adenoma and one case as Hashimoto's thyroiditis.

- Hence the suspicious results in FNAC prove to be an area of uncertainty often resolved by diagnostic surgical resection.

- In case of Multinodular goiter even if the preoperative FNAC is negative it does not exclude with certainty the possibility of a carcinoma because the error in sampling the right area is greater. Such

evaluation may lead to non radical operation and the need of a second surgery or radio therapy.

- For example in our study 8 cases reported as nodular colloid goiter in FNAC turned out to papillary carcinoma in 7 cases and medullary carcinoma in one case after HPE report.

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PROFORMA

PROFORMA

Name

Age

Sex

IPNO

Presenting Complaints

Swelling

- origin
- Duration
- Progress

Pain

Pressure effects

Toxic symptoms

Menstrual H/O

Obstetric H/O

H/O DM/HT/Tb

Family H/O

H/O Previous surgery

General examination

Pulse rate

B.P

Anemia

Cachexia

L/E

Systemic examination

CVS

RS

CNS

P/A

SKELETAL

ENT

Clinical diagnosis

Investigation

Lab :- Haemogram

Urine – Albumin , sugar

Blood – sugar, urea

T3T4 TSH

X ray chest

X ray Neck

USG Neck

FNAC

Treatment :- Surgery

Follow up :- Depends on HPE report

MASTER CHART